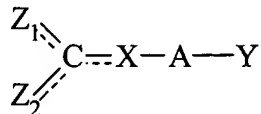


1. [Previously Presented] A method of increasing ATP production of a subject, comprising administering to said subject an effective amount of a creatine compound and an ATP enhancing agent, such that the ATP production is increased, wherein said creatine compound has the formula:



and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{C}(=\text{O})\text{NHSO}_2\text{J}$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, and C_1 - C_5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) $-\text{NH}-\text{M}$, wherein M is selected from the group consisting of: hydrogen, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_1 - C_4 alkoyl, C_3 - C_4 branched alkyl, C_3 - C_4 branched alkenyl, and C_4 branched alkoyl;

c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:

- 1) hydrogen;
 - 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
 - 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
 - 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z₁ and Z₂ are chosen independently from the group consisting of: =O, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =O and wherein R₂ is selected from the group consisting of:
- 1) hydrogen;
 - 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

- 4) a C₄-C₈ α-amino-carboxylic acid attached via the α-carbon;
- 5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;
- 6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P(=O))_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
- 7) -E, wherein E is selected from the group consisting of: -(P(=O))_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of - NHR_2 , $-CH_2R_2$ and $-NR_2OH$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

2. [Original] The method of claim 1, wherein said creatine compound is creatine.

3. [Original] The method of claim 1, wherein said creatine compound is cyclocreatine.

4. [Original] The method of claim 1, wherein said creatine compound is creatine phosphate.

Claim 5 (Cancelled).

6. [Currently Amended] The method of claim 1, wherein said ATP enhancing agent is a CoQ, ~~vitamin~~, spin trap, carnitine, antioxidant, vincopocetine or combination thereof.

7. [Original] The method of claim 6, wherein the agent is CoQ₁₀.

8. [Original] The method of claim 6, wherein the agent is carnitine.

Claim 9 (Cancelled).

10. [Original] The method of claim 6, wherein said antioxidant is pyruvate.

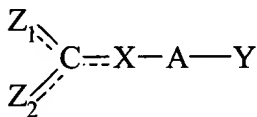
11. [Original] The method of claim 6, wherein the antioxidant is lutein.

12. [Original] The method of claim 6, wherein the agent is vinpocetine.

13. [Original] The method of claim 1, further comprising administering a herbal extract.
14. [Original] The method of claim 13, wherein the extract is rosemary or black caraway extract.
15. [Original] The method of claim 1, further comprising administering a berry oil or meal.
16. [Original] The method of claim 15, wherein said berry oil or meal is from blackberries, blueberries, black raspberries, or mixtures thereof.
17. [Original] The method of claim 1, wherein said subject is suffering or at risk of suffering from a nervous system disorder.
18. [Original] The method of claim 1, wherein said subject is human.

Claims 19-33 (Cancelled).

34. [Previously Presented] A method of protecting the nervous system of a subject against oxidative damage, comprising administering to said subject an effective amount of a creatine compound and a neuroprotective agent, such that the nervous system of the subject is protected against oxidative damage, wherein said creatine compound has the formula:



and pharmaceutically acceptable salts thereof, wherein:

- a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=O)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₅-C₉ α-amino-ω-methyl-ω-adenosylcarboxylic acid attached via the ω-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z₁ and Z₂ are chosen independently from the group consisting of: =O, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =O and wherein R₂ is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P(O)₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q,

where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OH})(\text{CH}_2)_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}_2\text{G}$, where G is independently selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, $\text{C}_4\text{-C}_6$ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of - $(\text{P}\text{O}_3)_n\text{NMP}$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OCH}_3)(\text{O})_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OH})(\text{CH}_2)_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}=\text{G}$, where G is independently selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, $\text{C}_4\text{-C}_6$ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

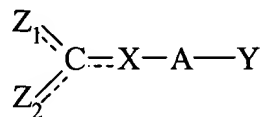
g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of - NHR_2 , $-\text{CH}_2\text{R}_2$ and $-\text{NR}_2\text{OH}$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

35. [Original] The method of claim 34, wherein said creatine compound is creatine.

36. [Original] The method of claim 34, wherein said creatine compound is cyclocreatine.
37. [Original] The method of claim 34, wherein said creatine compound is creatine phosphate.
38. [Original] The method of claim 34, wherein said neuroprotective agent is an anti-oxidant compound.
39. [Original] The method of claim 38, wherein said antioxidant is selected from the group consisting of vitamin E, lutein, pyruvate, alpha-omega fatty acids, BHP, alpha-lipoate, thiocetic acid, 1,2-dithiolane-3-pentanoic acid, 1,2-dithiolane-3 valeric acid, and 6,8-dithiooctanoic acid.

Claims 40-63 (Cancelled).

64. [Currently Amended] A method for treating amyotrophic lateral sclerosis in a subject, comprising:
- administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that amyotrophic lateral sclerosis in said subject is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:



and pharmaceutically acceptable salts thereof, wherein:

- a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=O)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₅-C₉ α-amino-ω-methyl-ω-adenosylcarboxylic acid attached via the ω-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z₁ and Z₂ are chosen independently from the group consisting of: =O, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =O and wherein R₂ is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P(O)₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via

the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-[P(=O)(OCH_3)(O)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, $-C(=O)G$, and $-CO_2G$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl, wherein E may be attached to any point to D , and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) $-E$, wherein E is selected from the group consisting of $-(P(O)_3)_nNMP$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-[P(=O)(OCH_3)(O)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, $-C(=O)G$, and $-CO=G$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

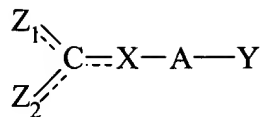
f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of $-NHR_2$, $-CH_2R_2$ and $-NR_2OH$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

65. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is a mitochondrial cofactor.

66. [Previously Presented] The method of claim 65, wherein said mitochondrial cofactor is 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone.
67. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is an electron transport chain regulator.
68. [Previously Presented] The method of claim 64, wherein said electron transport chain regulator is nicotinamide.
69. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is a spin trap.
70. [Previously Presented] The method of claim 69, wherein said spin trap is PBN.
71. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is a cofactor for normal cellular metabolism.
72. [Previously Presented] The method of claim 71, wherein said cofactor is carnitine.
73. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is an antioxidant.
74. [Previously Presented] The method of claim 73, wherein said antioxidant is vitamin E.
75. [Cancelled].
76. [Currently Amended] The method of claim ~~64~~75, wherein said neuroprotective agent~~vitamin~~ is riboflavin.
77. [Previously Presented] The method of claim 64, further comprising administering at least one additional neuroprotective agent or creatine compound.

78. [Previously Presented] The method of claim 64, wherein said creatine compound is creatine.
79. [Previously Presented] The method of claim 64, wherein said creatine compound is creatine phosphate.
80. [Previously Presented] The method of claim 64, wherein said creatine compound is cyclocreatine.
81. [Previously Presented] The method of claim 64, wherein said creatine compound is cyclocreatine phosphate.
82. [Previously Presented] The method of claim 64, wherein said creatine compound is homocyclocreatine.
83. [Previously Presented] The method of claim 64, wherein said subject is a mammal.
84. [Previously Presented] The method of claim 83, wherein said subject is a human.
85. [Cancelled].
86. [Currently Amended] A method for treating Parkinson's disease in a subject, comprising:
administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Parkinson's disease in said subject is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:



and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=O)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆

branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z₁ and Z₂ are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =0 and wherein R₂ is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{SO}_3\text{H}$, $-\text{NO}_2$, $\text{OP}(=\text{O})(\text{OH})(\text{OJ})$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C_1 - C_3 straight alkyl, C_3 branched alkyl, C_2 - C_3 straight alkenyl, C_3 branched alkenyl, C_1 - C_3 straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: $-(\text{P}(\text{O}_3))_n\text{NMP}$, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OCH}_3)(\text{O})_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OH})(\text{CH}_2)_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, $-\text{OG}$, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}_2\text{G}$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of: $(\text{P}(\text{O}_3))_n\text{NMP}$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OCH}_3)(\text{O})_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{P}(=\text{O})(\text{OH})(\text{CH}_2)_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: Cl, Br, epoxy, acetoxy, $-\text{OG}$, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}=\text{G}$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of - NHR_2 , $-CH_2R_2$ and $-NR_2OH$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

87. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is a mitochondrial cofactor.

88. [Previously Presented] The method of claim 88, wherein said mitochondrial cofactor is 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone.

89. [Previously Presented] The method of claim 88, wherein said neuroprotective agent is an electron transport chain regulator.

90. [Previously Presented] The method of claim 89, wherein said electron transport chain regulator is nicotinamide.

91. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is a spin trap.

92. [Previously Presented] The method of claim 91, wherein said spin trap is PBN.

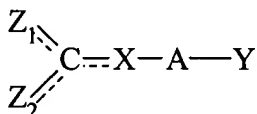
93. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is a cofactor for normal cellular metabolism.

94. [Previously Presented] The method of claim 93, wherein said cofactor is carnitine.

95. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is an antioxidant.

96. [Previously Presented] The method of claim 95, wherein said antioxidant is vitamin E.
97. [Cancelled]
98. [Currently Amended] The method of claim ~~86~~⁹⁷, wherein said neuroprotective agent~~vitamin~~ is riboflavin.
99. [Previously Presented] The method of claim 86, further comprising administering at least one additional neuroprotective agent or creatine compound.
100. [Previously Presented] The method of claim 86, wherein said creatine compound is creatine.
101. [Previously Presented] The method of claim 86, wherein said creatine compound is creatine phosphate.
102. [Previously Presented] The method of claim 86, wherein said creatine compound is cyclocreatine.
103. [Previously Presented] The method of claim 86, wherein said creatine compound is cyclocreatine phosphate.
104. [Previously Presented] The method of claim 86, wherein said creatine compound is homocyclocreatine.
105. [Previously Presented] The method of claim 86, wherein said subject is a mammal.
106. [Previously Presented] The method of claim 105, wherein said subject is a human.
107. [Cancelled].
108. [Currently Amended] A method for treating Huntington's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Huntington's disease, amyotrophic lateral sclerosis is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:



and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{C}(=\text{O})\text{NHSO}_2\text{J}$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, and C_1 - C_5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) $-\text{NH-M}$, wherein M is selected from the group consisting of: hydrogen, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_1 - C_4 alkoyl, C_3 - C_4 branched alkyl, C_3 - C_4 branched alkenyl, and C_4 branched alkoyl;

c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:

- 1) hydrogen;
- 2) K where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C_5 - C_9 a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C_5 - C_9 a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C_5 - C_9 a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z_1 and Z_2 are chosen independently from the group consisting of: $=\text{O}$, $-\text{NHR}_2$, $-\text{CH}_2\text{R}_2$, $-\text{NR}_2\text{OH}$; wherein Z_1 and Z_2 may not both be $=\text{O}$ and wherein R_2 is selected from the group consisting of:

- 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl; C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C_4 - C_8 α -amino-carboxylic acid attached via the ω -carbon;

5) B, wherein B is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{SO}_3\text{H}$, $-\text{NO}_2$, $\text{OP}(=\text{O})(\text{OH})(\text{OJ})$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;

6) $-\text{D-E}$, wherein D is selected from the group consisting of: C_1 - C_3 straight alkyl, C_3 branched alkyl, C_2 - C_3 straight alkenyl, C_3 branched alkenyl, C_1 - C_3 straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: $-(\text{P}(\text{O})_3)_n\text{NMP}$, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OCH}_3)(\text{O})]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OH})(\text{CH}_2)]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, $-\text{OG}$, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}_2\text{G}$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) $-\text{E}$, wherein E is selected from the group consisting of: $(\text{P}(\text{O})_3)_n\text{NMP}$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OCH}_3)(\text{O})]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OH})(\text{CH}_2)]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C_1 , Br, epoxy, acetoxy,

-OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;

f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R₁ is present and Z₁ or Z₂ is selected from the group consisting of -NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z₁ or Z₂ to form a cycle of 4 to 7 members.

109. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is a mitochondrial cofactor.

110. [Previously Presented] The method of claim 109, wherein said mitochondrial cofactor is 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone.

111. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is an electron transport chain regulator.

112. [Previously Presented] The method of claim 108, wherein said electron transport chain regulator is nicotinamide.

113. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is a spin trap.

114. [Previously Presented] The method of claim 113, wherein said spin trap is PBN.

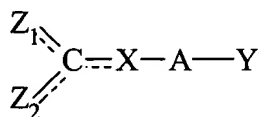
115. [Currently Amended] The method of claim 108, wherein said ~~cofactorneuroprotective agent~~ is a cofactor for normal cellular metabolism.

116. [Previously Presented] The method of claim 115, wherein said cofactor is carnitine.
117. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is an antioxidant.
118. [Previously Presented] The method of claim 117, wherein said antioxidant is vitamin E.
119. [Cancelled].
120. [Currently Amended] The method of claim 119, wherein said neuroprotective agent ~~vitamin~~ is riboflavin.
121. [Previously Presented] The method of claim 108, further comprising administering at least one additional neuroprotective agent or creatine compound.
122. [Previously Presented] The method of claim 108, wherein said creatine compound is creatine.
123. [Previously Presented] The method of claim 108, wherein said creatine compound is creatine phosphate.
124. [Previously Presented] The method of claim 108, wherein said creatine compound is cyclocreatine.
125. [Previously Presented] The method of claim 108, wherein said creatine compound is cyclocreatine phosphate.
126. [Previously Presented] The method of claim 108, wherein said creatine compound is homocyclocreatine.
127. [Previously Presented] The method of claim 108, wherein said subject is a mammal.

128. [Previously Presented] The method of claim 127, wherein said subject is a human.

Claim 129 (Cancelled).

130. [Currently Amended] A pharmaceutical composition for treating amyotrophic lateral sclerosis, Huntington's disease or Parkinson's disease ~~modulating a nervous system disease~~ in a subject, comprising
a synergistically effective amount of a combination of a creatine compound having the formula



and pharmaceutically acceptable salts thereof, ~~wherein said nervous system disease is amyotrophic lateral sclerosis, Huntington's disease or Parkinson's disease, and~~ wherein:

a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=O)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z₁ and Z₂ are chosen independently from the group consisting of: =O, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =O and wherein R₂ is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₄-C₈ α-amino-carboxylic acid attached via the α-carbon;

5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P(=O))_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of: -(P(=O))_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via

the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-[P(=O)(OCH_3)(O)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m-Q$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: C_1 , Br, epoxy, acetoxy, -OG, $-C(=O)G$, and $-CO=G$, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

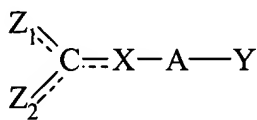
f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of -NHR₂, -CH₂R₂ and -NR₂OH, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members; and a neuroprotective agent and a pharmaceutically acceptable carrier, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10.

131. [Previously Presented] The pharmaceutical composition of claim 130, wherein said creatine compound is creatine.

132. [Currently Amended] A packaged composition~~nervous system disease modulator~~, comprising

a creatine compound having the formula



and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{C}(=\text{O})\text{NHSO}_2\text{J}$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, and C_1 - C_5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) $-\text{NH}-\text{M}$, wherein M is selected from the group consisting of: hydrogen, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_1 - C_4 alkoyl, C_3 - C_4 branched alkyl, C_3 - C_4 branched alkenyl, and C_4 branched alkoyl;

c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a $\text{C}_5\text{-C}_9$ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a $\text{C}_5\text{-C}_9$ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a $\text{C}_5\text{-C}_9$ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z_1 and Z_2 are chosen independently from the group consisting of: $=\text{O}$, $-\text{NHR}_2$, $-\text{CH}_2\text{R}_2$, $-\text{NR}_2\text{OH}$; wherein Z_1 and Z_2 may not both be $=\text{O}$ and wherein R_2 is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl; $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, and $\text{C}_4\text{-C}_6$ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a $\text{C}_4\text{-C}_8$ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{SO}_3\text{H}$, $-\text{NO}_2$, $\text{OP}(=\text{O})(\text{OH})(\text{OJ})$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_3\text{-C}_6$ branched alkenyl, and aryl, wherein B is optionally connected to

the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of:
-(P(=O))_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of -
(P(=O))_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;

f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of - NHR_2 , $-CH_2R_2$ and $-NR_2OH$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members; and a neuroprotective agent, both packaged with instructions for using an effective amount of a combination of the creatine compound and said neuroprotective agent as a ~~nervous system disease modulator, wherein said nervous system disease is~~ for the treatment of amyotrophic lateral sclerosis, Parkinson's disease or Huntington's disease, said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10.